Long-term outcome of splenectomy in Immunethrombocytopenia (ITP)

ABSTRACT

ITP is a chronic illness with frequent mucosal bleeding. Though the first line treatment is corticosteroids, relapse is frequent which necessitates splenectomy. Response to splenectomy is usually good initially; however, over the years relapses are frequent. Drugs then used are azathioprine, mycophenolate mofetil, anti-D globulin, TPO-receptor agonists, rituximab, cyclosporine, etc. Ultimately there is a small subset of patients who may require a small dose of prednisolone lifelong.

Introduction

The standard of carefor individuals with steroid-refractory ITP for many years was splenectomy. However, the situation has altered due to the rituximab and TPO-RAs (Thrombopoietin Receptor Agonists) availability.The first-line treatment for ITP is corticosteroids.Normally, a small dose of prednisolone is found good enough to give an adequate response to the patient.

However, after about a year of response,the platelet count drops again and the patient may have spontaneous mucosal bleeding like gum bleed, epistaxis, etc. Few female patients may have increased menstrual bleeding. All these progresses suggest a patient may develop refractory ITP. Splenectomy should be taken into account in this case due to the spleen's tendency for excessive platelet destruction.

Splenectomy Efficiencyfor ITP

Platelet counts rise right post-splenectomy, and patients experience long-lasting remission in the majority of ITP patients.[1,2,3] In a study of published case series from1966 to 2004, 1731 (66 percent) of 2623 individuals kept a full response after a median of twenty-nine months of follow-up [4].

Twenty to thirty percent of individuals experience post-splenectomy relapses during the first 24 months.[5] However, they respond to alternative treatment. A small proportion of patients experience high mortality andmorbidity.[5]

The International Working Group Consensus survey [7] and ASH ("American Society of Hematology") in 2011 [6] both propose splenectomy as 2ndline treatment for ITP. However,Splenectomy is more strongly suggested by ASH guidelines.

Predictors of splenectomy response

Splenectomy outcomes are unpredictable, and data on response rates pertain to peopleinstead of specific patients. Splenectomy response predictors were assessedas follows below: It has been suggested that the initial week following splenectomy might indicate long-term response.

Complications connected with splenectomy might be infections. It is widely known that asplenic patients run the risk of developing severe bacterial sepsis [7]. This risk was decreased from about7.16/100 to 2.3/100 patientyears with pre-splenectomy vaccination [8].

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Platelet scintigraphy

IIndium-labeled autologous platelet scanning, in which the patient receives [9] In-labeled autologous platelets and following scintigraphy determines the location of platelet clearance,[10] has become an effective predictor of "splenectomy" response but was not yet attained broad recognition. A splenectomy response was seen in 91.4 percent (range between 87.0-94.8 percent) of people with a "splenic pattern" and 40.9 percent (range between 15.4-100 percent) of peoplehaving adiffuse, mixed, or hepatic pattern within a pooled study of6cases (n=580).[11-12]

Pondicherry experience, India [13]

AIM: Splenectomy is the recommended 2nd line therapy for chronic immunological thrombocytopenic purpura after corticosteroids fail to control the condition. Splenectomy has a 50–60percent success rate in obtaining complete remission. However, the real long-term result is uncertain because the majority of follow-ups are less than five years, as per cited articles. This retrospective analysis of adult peoplehaving chronic ITP evaluates the genuine long-term result of splenectomy across a long time and the determinants of splenectomy response.

METHODS: We studied the medical records of 49 patients at a reputed institution in southern India who just had a splenectomy for chronic ITP between 1982 and 2015 [Range between 2 to 396 months (33years)]. The average duration of observation was 75.71 months.

RESULTS: Splenectomy response decreased from 83.3percent (5 out of 6 patients) after 1 year to 25 percent (1 out of four patients) when evaluated after fifteen years. There was no statistically substantialcorrelation between any of the examined variables, including age, gender, the first reaction to steroids ("pre-operative"), long-term remission, as well aspost-operative platelet count.

Nevertheless, Individuals having“post-splenectomy” recurrence may be treated with a much lower dosage of prednisolone (16.7 mg per day) than their typical pre-splenectomy demand (47.5mg per day).

CONCLUSION: Even though splenectomy temporarily “normalizes platelet count”, maintained long-term remission gradually declines with time; just one-third of patients may still be in remission by the ten years following surgery. Furthermore, no element could predict how a splenectomy would respond.

A review by Vesely SK et al [14]

90 publications with 656 splenectomized patients treated with 22 treatments were examined in a systematic review by Vesely SK et al. The greatest complete responses were recorded with azathioprine, cyclophosphamide, and rituximab, although only in 41-109 individuals. The reported full response rates varied from 17-27%, although 36-42percent of patients with such three therapies did not respond. Most publications solely discussed platelet count responses; only 63 patients' bleeding outcomes were mentioned (10 percent). The only individuals with a pretreatment platelet count less than10×10^9 cells/L were 111 (17%) of the 656 eligible patients.

The authors found that there is insufficient data to help the efficacy of any therapy for individuals with chronic severe thrombocytopenia and ITPfollowing splenectomy. Randomized, controlled trials should be used to assess potentially beneficial therapies for both benefit and safety.

Review by Bell et al [15]

Long-term effects of ITP splenectomy

ITP is predominantly an acquired thrombocytopenia-related condition that does not include marrow failure. Splenectomy was initially utilized in 1913 to treat ITP.With the discovery that opsonin (crucial for the optimum elimination of invading microorganisms with white blood cells is produced within the spleen, spontaneous splenic excision has beenquestioned andreassessed. The success

rateof Splenectomyis approximatelyconstant (approximately 50 and 60 percent), regardless of whether it is carried out very early after diagnosis or several months or years afterward.

Perspective: deciding on splenectomy

In general, it is advised splenectomy should be deferred at least for a year after the onset of illness, since there may be spontaneous remission.

There are several situations in which splenectomy should be considered.Patients may have severe ITP, which is characterized by severe bleeding, profound "thrombocytopenia", a poor or temporary response to IVIg andcorticosteroids, as well as a suboptimal reaction to TPO-RA. Splenectomy is performed for express relief.

Conclusion

ITP is a benign recurrent bleeding disorder that responds to steroids initially very well. However, relapses are common which warrant consideration of splenectomy later. Nevertheless,the long-term effect of splenectomy might not be very satisfying in all cases; and patients may require subsequent treatment with oral drugs like rituximab, TPO-R agonists, cyclosporine, low dose steroids,etc.

References

1. Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. *Blood*. 2004;104:2623-2634.

2. Kumar S, Diehn FE, Gertz MA, Tefferi A. Splenectomy for immune thrombocytopenic purpura: long-term results and treatment of post-splenectomy relapses. *Ann Hematol*. 2002;81:312-319.

3. Palandri F, Polverelli N, Sollazzo D, et al.. Have splenectomy rates and main outcomes of ITP changed after the introduction of new treatments? A monocentric study in the outpatient setting during 35 years. *Am J Hematol*. 2016;91(4):E267-E272.

4.. Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. *Blood*. 2004;104:2623-2634.

5.. McMillan R, Durette C. Long-term outcomes in adults with chronic ITP after splenectomy failure. *Blood*. 2004;104:956-960.

6.. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA; American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117:4190-4207.

7.. Eraklis AJ, Kevy SV, Diamond LK, Gross RE. Hazard of overwhelming infection after splenectomy in childhood. *N Engl J Med*. 1967;276:1225-1229.

8. Ejstrud P, Kristensen B, Hansen JB, Madsen KM, Schønheyder HC, Sørensen HT. Risk and patterns of bacteraemia after splenectomy: a population-based study. *Scand J Infect Dis*. 2000;32:521-525.

9. Cines DB, Levine LD. Thrombocytopenia in pregnancy. *Blood*. 2017;130(21):2271-2277.

10. Patel VL, Mahevas M, Lee SY, et al.. Outcomes 5 years after response to rituximab therapy in children and adults with immune thrombocytopenia. *Blood*. 2012;119(25):5989-5995.

11. Tarantino MD, Bussel JB, Blanchette VS, et al.. Romiplostim in children with immune thrombocytopenia: a phase 3, randomized, double-blind, placebo-controlled study. *Lancet*. 2016;388(10039):45-54.

12. Gonzalez-Porras JR, Escalante F, Pardal E, et al.; Grupo de Trombosis Hemostasia de Castilla y León. Safety and efficacy of splenectomy in over 65-yrs-old patients with immune thrombocytopenia. *Eur J Haematol*. 2013;91(3):236-241

13. Dutta TK, Diljith H, Vishnu VY, Verma SP, Charles Deepak, Vinod KV, Basu D. Long-Term Outcome of Splenectomy in Chronic Immune Thrombocytopenic Purpura. International Journal of HematologyResearch 2017; 3:164-167

14. Vesely SK, Jedidiah J Perdue, Mujahid A Rizvi, Deirdra R Terrell, James N George. Management of adult patients with persistent idiopathic thrombocytopenic purpura following splenectomy: a systematic review. Annals of Internal Medicine 2004; 20: 112-20

15. W R Bell Jr. Long-term outcome of splenectomy for idiopathic thrombocytopenic purpura. Semin Hematol. 2000; 37(1 Suppl 1): 22-5.

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